solution was cooled to 0°–5° C., and methyl bromide (1.0 mL, 28 mmol) and KOH (0.2 g, 3.0 mmol) were added in that order. The reaction mixture was stirred for 1 hour, the reaction was diluted by addition of 50 mL of heptane, and 10 mL of 2N NaOH were added to quench the reaction. The layers were separated, a gummy by-product was collected, and the organic layer was washed with water. The heptane layer was dried over MgSO4, and the solvent was removed under vacuum to afford 1.54 g of 6-O-methyl-2'-TMS-erythromycin A oxime IPCH ketal (69% yield). The gummy by-product was dissolved in 50 mL of isopropyl acetate. The solution was dried and filtered, and the solvent was removed under vacuum to give 0.36 g of a material identified as a quaternary salt by NMR spectroscopy. See Table 4 below for a summary of Examples 9 and 10.

Example 10

Methylation of mono-protected 2'-TMS-erythromycin A oxime IPCH ketal:

Methylation procedure with KOH and TEA

The procedure of Example 9 was followed, except that the order of addition of reagents to the solution of starting material was TEA (1.75 g, 17.3 mmol), methyl bromide (0.5 mL, 9.0 mmol), then KOH (0.23 g, 3.0 mmol), to afford 1.84 g of the desired product, 6-O-methyl-2'-TMS-erythromycin A oxime IPCH ketal (74.5% yield), and 0.1 g of the quaternary by-product. See Table 4 below for a summary of Examples 9 and 10.

TABLE 4

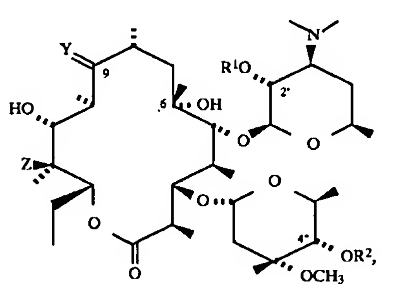
Summary of Examples 9 and 10.

Ex. No.	Base	starting material (mmol)	6-O-methyl prod (g)	yield (%)
9	KOH	2.2	1.54	69
10	KOH + TEA	2.2	1.84	74.5

These data demonstrate that higher yields of 2'-mono-protected product are obtained in the presence of TEA.

We claim:

1. An improved process for selective alkylation of a hydroxy group at the 6-position of a compound of the formula:



wherein:

R^1 and R^2 are independently hydrogen or a hydroxy-protecting group, except that R^1 and R^2 may not both be hydrogen simultaneously;

Y is selected from the group consisting of:

a) oxygen,

b) an oxime having the formula N-O-R^3, wherein R^3 is selected from the group consisting of:

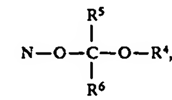
hydrogen,

a loweralkenyl group,

an aryl(loweralkyl) group, or

a substituted aryl(loweralkyl) group; and

c) an oxime having the formula:



wherein

R^4 is a loweralkyl group,

a cycloalkyl group;

a phenyl group,

an aryl(loweralkyl) group;

or R^4 and R^5 or R^4 and R^6 and the atoms to which they are attached are taken together form a 5- to 7-membered ring containing one oxygen atom;

R^5 is a loweralkyl group,

a loweralkoxymethyl group;

or R^5 and R^4 and the atoms to which they are attached are taken together form a 5- to 7-membered ring containing one oxygen atom,

or R^5 and R^6 and the atoms to which they are attached are taken together form a 5- to 7-membered cycloalkyl group; and

R^6 is a hydrogen atom,

a loweralkyl group,

a phenyl group,

an aryl(loweralkyl) group;

or R^6 and R^4 and the atoms to which they are attached are taken together form a 5- to 7-membered ring containing one oxygen atom;

or R^6 and R^5 and the atoms to which they are attached are taken together form a 5- to 7-membered cycloalkyl group;

with the requirement that only one pair of substituents (R^4 and R^5), (R^4 and R^6) or (R^5 and R^6) may be taken together with the atoms to which they are attached to form a ring as defined above; and

Z is hydrogen, hydroxy or protected-hydroxy;

comprising reacting the compound with an alkylating agent in the presence of both a strong alkali metal base and a weak organic amine base in polar aprotic solvent or a mixture of polar aprotic solvents maintained at a reaction temperature for a period of time sufficient to complete the alkylation, by adding the weak organic base prior to the addition of the alkylating agent and the strong alkali metal base.

2. The process according to claim 1, wherein the weak organic amine base is selected from the group consisting of trimethyl-amine, triethylamine, tripropylamine, pyridine, 2-methoxypyridine, 1-methyl-pyrrolidine, 1-methylpiperidine, and 1-ethylpiperidine.

3. The process according to claim 1, wherein the alkylating agent is selected from the group consisting of methyl bromide, methyl iodide, dimethyl sulfate and methyl-p-toluenesulfonate.

4. The process according to claim 1, wherein the solvent is a mixture of solvents selected from the group consisting of N,N-dimethyl-formamide, dimethyl sulfoxide, N-methyl-2-pyrrolidone, hexamethylphosphoric triamide, tetrahydrofuran, 1,2-dimethoxyethane, acetonitrile and ethyl acetate.

5. The process according to claim 1, wherein R^1 and R^2 in the compound are independently hydrogen or a hydroxy-protecting group, which is benzyloxycarbonyl, acetyl, or a substituted silyl group of formula $SiR^7R^8R^9$, wherein R^7, R^8 and a R^9 are the same or different and each is a hydrogen

atom, a loweralkyl group, a phenyl-substituted alkyl group in which the alkyl moiety has 1 to 3 carbon atoms, a phenyl group, a cycloalkyl group having 5 to 7 carbon atoms, or a loweralkenyl group having 2 to 5 carbon atoms; with the provisions that at least one of R^7, R^8 and R^9 is not a hydrogen atom.

6. The process according to claim **1**, wherein the compound is 2' mono trimethylsilyl erythromycin A oxime

isopropyl cyclohexyl ketal, or 4" monotrimethylsilyl erythromycin A oxime isopropyl cyclohexyl ketal.

7. The process according to claim **1**, wherein the compound is a mixture of 2' mono trimethylsilyl erythromycin A oxime isopropyl cyclohexyl ketal and 4" monotrimethylsilyl erythromycin A oxime isopropyl cyclohexyl ketal.

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